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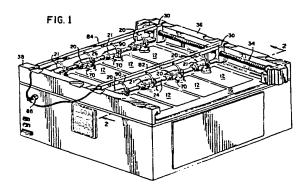
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Processing apparatus for a chemical reaction pack.

(57) Disposable reaction packs for use in automatic analysis equipment are known. These packs comprise a body which is divided into successive chambers, each of which contains a fluid. Mixing of the fluids in such packs is achieved by manually applying pressure to each chamber of the reaction pack to open the seal between each chamber. This process is time-consuming, inaccurate and could result in damage to the reaction pack. Described herein is apparatus (10) for transferring liquid from one chamber to another in successive chambers of a chemical reaction pack (12). The apparatus (10) comprises a support surface (16) on which the packs (12) are placed, and a plurality of pressure applicators (20) which are driven to apply pressure to the packs (12). Temperature control elements (70) are also provided to heat and cool the liquid contained within each chemical reaction pack (12).



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PROCESSING APPARATUS FOR A CHEMICAL REACTION PACK

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The present invention relates to processing apparatus for chemical reaction packs, and is more particularly concerned with the progressive transfer of a test fluid between adjacent chambers of the chemical reaction pack.

Disposable reaction packs for use in automatic analysis equipment are known in the art. Such reaction packs typically comprise a body fabricated from flexible pliable material. The body of the reaction pack is divided into successive individual compartments or chambers having blister-like configurations which are normally separated from each other with seals which are rupturable or openable in response to a sufficient pressure being applied to such seals. One or more of the compartments or chambers contain predetermined amounts of reagents with which a test liquid reacts.

By applying an external linearly advancing pressure to the blister-like chambers, the normally closed seals are opened to permit transfer of the contents of a preceding chamber to a succeeding chamber. Such a technique is disclosed in US-A-3036894. The transfer of the test liquid between chambers and the intermixing thereof with the reagents is preferably accomplished without opening the reaction pack.

Manually applying an external pressure to each blister-like chamber of the reaction pack to establish sufficient internal pressure to open the normally closed seal is tedious, time-consuming, inexact, and could result in damage to the reaction pack. Inconsistency or variations in pressure and time can adversely effect chemical reactions within the pack and lead to inaccurate results. It would be beneficial, therefore, to automate the process of facilitating transfer of test liquids through a reaction pack.

The test liquids in the reaction pack may be subjected to temperature changes during the test procedure. It has been found, for example, that thermal cycling by heating and cooling a metal block on which a reaction pack is situated is relatively slow and inefficient.

Accordingly, a problem exists in providing a device which automatically transfers a test liquid through a reaction pack with consistency while facilitating heating and cooling thereof to treat the liquids contained therewithin.

It is therefore an object of the present invention to provide a device which overcomes the problems mentioned above.

In accordance with one aspect of the present invention, there is provided processing apparatus for transferring a fluid between chambers in a chemical reaction pack, the pack having blister-like

chambers formed therein, the apparatus compris-

a support surface for supporting at least one chemical reaction pack in a substantially horizontal plane;

at least one pressure applicator supported above the support surface for acting on an associated reaction pack to transfer fluid between adjacent chambers; and

operating means for moving each pressure applicator through a range of movement extending across the associated reaction pack;

characterized in that the operating means comprises a shaft having at least one pressure applicator arranged thereon, the shaft advancing each pressure applicator across the support surface while maintaining a substantially constant orientation between each pressure applicator and the support surface.

In accordance with another aspect of the present invention, there is provided processing apparatus for transferring a fluid between blister-like chambers in a chemical reaction pack comprising: a support surface for supporting a plurality of the reaction packs in side-by-side and end-to-end relation relative to each other;

at least one roller supported above the support surface and in alignment with the blister-like configurations on the reaction packs; and

drive mechanism means for moving the rollers across the support surface to operate against the reaction packs and facilitate transfer of fluid therethrough;

characterized in that the drive mechanism means comprises at least two spaced apart generally parallel shafts each having a series of the rollers arranged endwise thereon;

and in that the drive mechanism means advances the shafts with the rollers arranged thereon across the support surface while maintaining a substantially constant orientation relative to the support surface.

In a preferred embodiment, the pressure applicators include a series of rollers which are arranged endwise on a shaft forming part of the drive mechanism. The drive mechanism advances the shaft with the rollers across the support surface while maintaining a substantially constant orientation between the shaft and the support surface.

Still further, the preferred embodiments feature a drive mechanism comprising a bracket supported at one end of the shaft and an axially elongated worm gear which extends in a direction generally orthogonal to the shaft and threadably engaging the bracket. The drive mechanism further includes

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a device for rotatably driving the worm gear to move the shaft. A rack and pinion arrangement is provided at opposite ends of the shaft. As the shaft moves, it is maintained generally perpendicular to the axis of the reaction packs irrespective of where the driving force is applied by the worm gear and which of the rollers runs into resistance from the blister-like chambers on the reaction pack.

To promote temperature changes of the liquids within the disposable reaction pack, temperaturecontrolling elements are mounted for movement in front of and with the rollers. Each temperaturecontrolling element includes upper and lower units. In a start position, the upper unit of the element is positioned temperature-controlling above a similar unit disposed beneath the support surface so that the two units can work together to provide the necessary heating and cooling cycle for the liquids in the reaction pack. When the rollers are moved, the upper unit is moved with the rollers and is positioned over the next blister-like chamber in the reaction pack. After the start position, all subsequent chambers in the reaction pack are treated by the temperature-control element from the top only. As will be understood, heating may either be at a constant temperature or a heating/cooling cycle.

The apparatus of the present invention allows each of the reaction packs arranged on the support surface to be treated with constant pressures on a generally flat surface for uniform time periods. Moreover, the present invention automates and simplifies handling of chemical reaction packs. When a temperature-control element is arranged in combination therewith, temperature of the test liquid in the reaction packs can be controlled during transfer of the test liquid between chambers.

The present invention will now be described by way of example only with reference to the accompanying drawings in which:

Figure 1 is a perspective view of apparatus embodying principles of the present invention and which is capable of operating upon a plurality of chemical reaction packs;

Figure 2 is a sectioned side view taken along line 2-2 of Figure 1;

Figure 3 is an enlarged view of a portion of a drive mechanism forming part of the present invention:

Figure 4 is a top plan view of the apparatus of the present invention; and

Figure 5 is an enlarged sectional view taken along line 5-5 of Figure 4.

While the present invention is susceptible of embodiment in various forms, there is shown in the drawings and will hereinafter be described a presently preferred embodiment with the understanding that the present disclosure is to be considered as an exemplification of the invention, and is not intended to limit the invention to the specific embodiment illustrated.

Referring now to the drawings, wherein like reference numerals refer to like parts throughout the several views, there is illustrated an apparatus 10 for operating on one or more chemical reaction packs 12. Each chemical reaction pack 12 comprises a sealed hollow body formed from fluid impermeable pliable material which is separated or divided into a series of aligned chambers; each chamber having a blister-like configuration. A test liquid is contained within one of the chambers and suitable reagents are contained within other chambers.

A more detailed description of a preferred form of reaction pack is provided in co-pending European patent application filed concurrently herewith, entitled "Temperature Control Device and Reaction Vessel".

The apparatus 10 of the present invention is preferably constructed as a self-contained unit including a base assembly 14 having a supporting surface 16 for supporting the chemical reaction packs 12 thereon in a substantially horizontal plane. As illustrated in figures 1 and 4, support surface 16 is preferably sized to accommodate a plurality of chemical reaction packs 12 in side-byside and end-to-end relation relative to each other.

Apparatus 10 includes pressure applicators 20 arranged above the support surface 16 of base assembly 14. In a preferred form, each pressure applicator 20 comprises a roller 21 located a predetermined distance above the support surface 16 for applying external pressure to a reaction pack 12 to transfer the liquid contained in the pack from one chamber to another.

Each roller 21 is moved through a range of movement extending endwise across the reaction packs by a drive mechanism 22. As best illustrated in Figure 2, drive mechanism 22 includes an elongated shaft 24 extending above and laterally across the support surface 16. A first series of rollers 21 are arranged endwise and freely rotatable on shaft 24.

To facilitate an increase in the capacity of the apparatus 10, another elongated shaft 26 (Figure 1) extends above and laterally across the support surface 16. Shafts 24 and 26 extend substantially parallel to each other and to the support surface 16. A second series of rollers 21 are arranged endwise and freely rotatable on shaft 26.

The drive mechanism 22 moves the shafts 24 and 26 with the rollers 21 mounted thereon across support surface 16. In a preferred form, the drive mechanism 22 conjointly moves both shafts 24 and 26 and the rollers supported thereon. The apparatus can be readily modified to operate shaft 24 with

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a first series of rollers 21 supported thereon independently of shaft 26 which has a second series of rollers 21 supported thereon.

The drive mechanism 22 and its relative association with shaft 24 will be described in detail with the understanding that similar construction is provided for shaft 26 and/or other shafts which support rollers 21 thereon.

As illustrated in Figure 3, the drive mechanism 22 includes a non-rotatable bracket 32 supported at one end of shaft 24. An axially elongated worm gear 34 extends in a direction generally orthogonal to the shaft 24 and threadably engages and passes through bracket 32. Opposite ends of the worm gear 34 are rotatably journalled in opposite ends of an upright support 36 connected to the base assembly 14 and extending generally parallel to the worm gear 34. Another upright support 38 (Figure 2) similar to support 36 is provided at the opposite end of shaft 24. A motor 40 (Figure 4) is fixedly supported on base assembly 14 for rotatably driving the worm gear 34 in opposite directions to effect linear movement of the shaft 24, thereby moving rollers 21 through their range of movement across the support surface 16.

The drive mechanism 22 is designed to facilitate programming of the apparatus and to allow each of the rollers 21 co-equally act on each reaction pack 12 during their range of movement. To effect such ends, and as illustrated in Figure 2, drive mechanism 22 includes rack and pinion assemblies 44 and 46 arranged at opposite ends of shaft 24 and extending substantially perpendicular or orthogonal thereto.

Alternatively, packs 12 can be operated upon randomly, if so desired.

As illustrated in Figure 3, rack and pinion assembly 44 includes a gear rack 48 and a pinion gear 50 accommodated within a cavity 51 defined in support 36. Gear rack 48 is arranged endwise on support 36 and extends parallel to the worm gear 34. Pinion gear 50 is pinned or otherwise affixed to one end of shaft 24.

Similarly, and as illustrated in Figure 2, rack and pinion assembly 46 includes a gear rack 52 and a pinion gear 54 accommodated within a cavity 55 defined in support 38. Gear rack 52 is arranged on support 38 and extends parallel to gear rack 48. Pinion gear 54 is pinned or otherwise affixed to the opposite end of shaft 24.

Drive mechanism 22 further comprises bearings 56 and 58 provided at opposite ends of shaft 24. As illustrated in Figure 2, bearings 56 and 58 are entrapped between respective upper guide faces 60 and 62 defined on respective supports 36 and 38, and respective elongated lower rails 64 and 66. Each rail 64 and 66 is fixed relative to the support surface 16. Accordingly, the horizontal axis

of shaft 24 about which rollers 21 move during their range of movement is maintained substantially parallel to and in a constant orientation with the support surface 16.

The apparatus 10 of the present invention further includes a plurality of temperature-controlling elements for providing rapid temperature changes in the fluid contained within the reaction pouch. As illustrated in Figure 1, a first series of temperature-controlling elements 70 are associated with shaft 24, while a second series of temperature-controlling elements 70 are associated with shaft 26. Each temperature-controlling element 70 is efficient, inexpensive and capable of rapidly moving the temperature of 140µl of liquid from 95 °C to 55 °C to 70 °C and back to 95 °C in a time period of from 45s to 105s (0.75min to 1.75 min) with a dwell time of at least 3s at each of these temperatures.

Turning to Figure 5, in a preferred form, each temperature-control element 70 includes an upper unit 72 and a lower unit 74. Each upper unit of the temperature-control elements 70 is supported in substantially the same manner. Accordingly, only a temperature-control element 70 as mounted to shaft 24 will be described in detail. Each upper unit 72 is carried in advance of and in alignment with a pressure applicator 20. A suitable cantilevered bracket 76 serves to mount the upper unit 72 to the shaft 24. Accordingly, when the pressure applicator 20 is moved through its range of movement the upper unit 72 of the temperature control element 70 moves therewith.

As illustrated in Figure 5, the support surface 16 defines a series of apertures 80 (only one of which is shown) which permit the lower heating unit 74 of the temperature control element to provide the necessary heating cycle to a lower surface of the chemical reaction pack 12. Additional heaters (not in the path of the pressure applicators 20) are provided as necessary for areas of the reaction pack which must be maintained at substantially constant temperature to receive the liquid warmed by the upper heater unit 72.

As illustrated in Figures 1 and 2, a pair of elongated tubular members 82 and 84 extend generally parallel to and in vertically spaced relation with shafts 24 and 26 respectively. The tubular members 82 and 84 are supported at one end by the non-rotatable brackets 32 of the drive mechanism 22. Support members 86 and 87, which are carried by the respective shafts 24 and 26, vertically support the other end of tubes 82 and 84. Accordingly, tubes 82 and 84 move with their respective shafts 24, 26 as the pressure applicators 20 move through their range of movement.

Tube 82 and 84 are connected to a source of cooling air 88 (Figure 1). Moreover, tubes 82 and 84 have a series of conduits 90 (Figures 1 and 5)

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which direct the cooling air from the tubes 82 and 84 to the various temperature-control elements 70 to provide the gradients in temperatures required.

Base assembly 14 further contains a computer, temperature measurement circuits, heater and motor drive circuits, and power supplies (not shown). A computer program controls functioning of the apparatus 10 and allows for changes to the operating parameters. An internal filter/regulator and solenoid valve will provide control to the air directed to the temperature-control element 70.

Transfer of the reagents in the chambers of the reaction packs is achieved by the action of the pressure applicators 20 against the blister-like chambers in the reaction packs. In the start position, the upper and lower units 72 and 74 of each temperature-control element are positioned to provide the necessary heating and cooling cycle for the liquid in the reaction pack. As the pressure applicators 20 linearly move through their range of movement, each roller 21 applies an external pressure against the reaction pack to transfer the liquid from one chamber to an adjacent chamber. Moreover, as the pressure applicators are moved, the upper unit 72 of each temperature-control unit 70 is pushed before the pressure applicator and is positioned over a succeeding chamber in the reaction pack which requires heating. After the start position, all subsequent chambers in the reaction packs are heated from the top only.

To effect movement of the pressure applicators 20 in either direction, motor 40 is suitably operated to rotatably drive the worm gear 34. Engagement between worm gear 34 and each of the non-rotatable brackets 32 in the drive mechanism 30 causes linear displacement of the brackets and thereby the shafts 24 and 26 connected thereto.

To simplify control of the apparatus 10 and to ensure that corresponding chambers in each reaction pack are activated simultaneously for an equivalent time period, drive mechanism 22 is designed such that shafts 24 and 26 and the pressure applicators 20 carried thereby maintain a substantially constant orientation relative to the support surface 16. The rack and pinion assemblies 44 and 46 associated with each shaft 24 and 26 of the drive mechanism are provided to effect such ends. Each gear rack 48 and 52 is held stationary above the support surface 26. Each pinion gear 50 and 54 which intermeshes with the racks 48 and 52, respectively, is therefore caused to rotate upon linear movement of the shafts 24 and 26 with the rollers 21 attached thereto. Because each pinion gear is affixed to an end of a respective shaft, rotational movement imparted to the pinion gear is likewise imparted to the shaft. Accordingly, each shaft is positively driven at both ends and is maintained substantially perpendicular to the longitudinal axis of the packets regardless of where a driving force is applied thereto and regardless of which of the rollers 21 carried thereon runs into resistance from the reaction pouch.

Moreover, the bearings 56 and 58 arranged at opposite ends of each shaft 24 and 26 further promote and maintain a substantially constant orientation between the pressure applicators 20 and the support surface 16. The ability to maintain a constant orientation between the pressure applicators 20 and the support surface 16 simplifies the control of the apparatus 10 and allows each of the packs to be co-equally acted upon for equal time periods, thereby facilitating handling of the reaction packs.

Claims

1. Processing apparatus for transferring a fluid between chambers in a chemical reaction pack, the pack having blister-like chambers formed therein, the apparatus comprising:-

a support surface (16) for supporting at least one chemical reaction pack (12) in a substantially horizontal plane;

at least one pressure applicator (20, 21) supported above the support surface (16) for acting on an associated reaction pack (12) to transfer fluid between adjacent chambers; and

operating means (22, 24, 26, 32, 34, 36, 38, 40, 44, 46, 48, 50, 52, 54, 56, 58, 64, 66) for moving each pressure applicator (20, 21) through a range of movement extending across the associated reaction pack (12);

characterized in that the operating means (22, 24, 32, 34, 36, 38, 40, 44, 46, 48, 50, 52, 54, 56, 58, 64, 66; 26) comprises a shaft (24; 26) having at least one pressure applicator (20, 21) arranged thereon, the shaft (24; 26) advancing each pressure applicator (20, 21) across the support surface (16) while maintaining a substantially constant orientation between each pressure applicator (20, 21) and the support surface (16).

2. Processing apparatus according to claim 1, wherein the operating means further comprises a non-rotatable bracket (32) supporting one end of the shaft (24; 26), an axially elongated worm gear (34) extending in a direction generally orthogonal to the shaft (24; 26) and threadably engaging the bracket (32), and drive means (40) for rotatably driving the worm gear (34).

3. Processing apparatus according to claim 1 or 2, wherein the operating means further includes rack and pinion means (44, 46, 48, 50, 52, 54) arranged at opposite ends of the shaft (24; 26) for ensuring that the shaft (24; 26) advances across the support surface (16) while maintaining a sub-

stantially constant orientation with the support surface (16) throughout the range of movement of each pressure applicator (20, 21).

- 4. Processing apparatus according to claim 3, wherein the rack and pinion means comprises a gear rack (48, 52) extending generally orthogonal to the shaft (24; 26), and a pinion gear (50, 54) intermeshed with the rack (48, 52) and mounted on the shaft (24; 26).
- 5. Processing apparatus according to claim 4, wherein the operating means further includes bearing means (56, 58) carried by the shaft (24; 26) for facilitating its movement across the support surface (16).
- 6. Processing apparatus according to claim 5, wherein the operating means further includes a rail (64, 66) adjacent to the gear rack (48, 52) and fixedly arranged relative to the support surface (16) so that the bearing means (56, 58) carried by the shaft (24; 26) rides on the rail (64, 66).
- 7. Processing apparatus according to any one of the preceding claims, further including temperature-control elements (70, 72) movable with the pressure applicators (20, 21) and operable upon the reaction pack (12) to change its temperature.
- 8. Processing apparatus according to claim 7, wherein the support surface (16) is apertured to accommodate temperature-control elements (74) beneath the reaction packs (12).
- 9. Processing apparatus for transferring a fluid between blister-like chambers in a chemical reaction pack comprising:
- a support surface (16) for supporting a plurality of the reaction packs (12) in side-by-side and end-toend relation relative to each other;
- at least one roller (20, 21) supported above the support surface (16) and in alignment with the blister-like configurations on the reaction packs (12); and
- drive mechanism means (22, 24, 26, 32, 34, 36, 38, 40, 44, 46, 48, 50, 52, 54, 56, 58, 64, 66) for moving the rollers (20, 21) across the support surface (16) to operate against the reaction packs (12) and facilitate transfer of fluid therethrough;
- characterized in that the drive mechanism means (22, 24, 26, 32, 34, 36, 38, 40, 44, 46, 48, 50, 52, 54, 56, 58, 64, 66) comprises at least two spaced apart generally parallel shafts (24, 26) each having a series of the rollers (20, 21) arranged endwise thereon:
- and in that the drive mechanism means (22, 24, 26, 32, 34, 36, 38, 40, 44, 46, 48, 50, 52, 54, 56, 58, 64, 66) advances the shafts (24, 26) with the rollers (20, 21) arranged thereon across the support surface (16) while maintaining a substantially constant orientation relative to the support surface (16).

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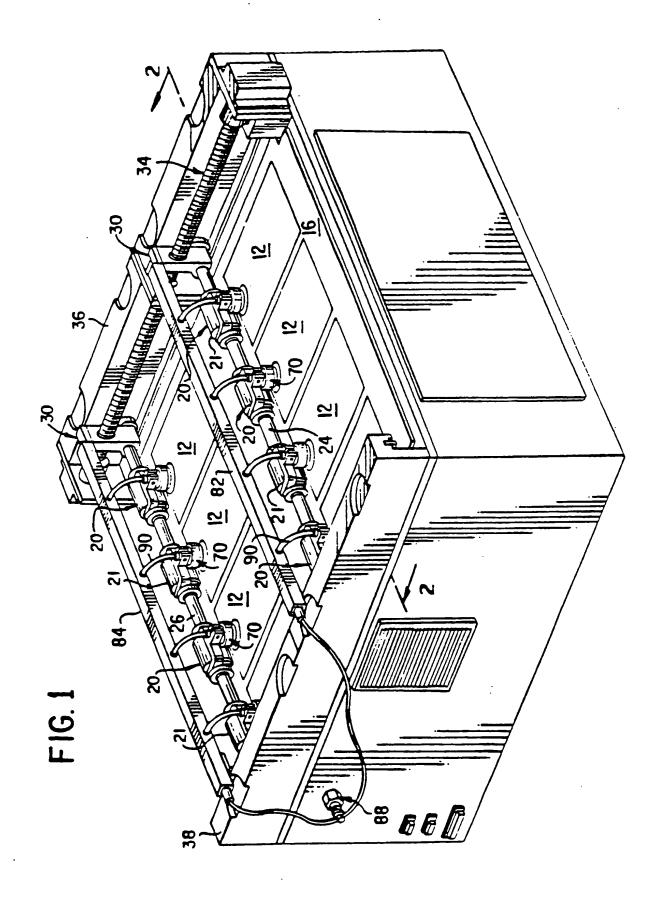
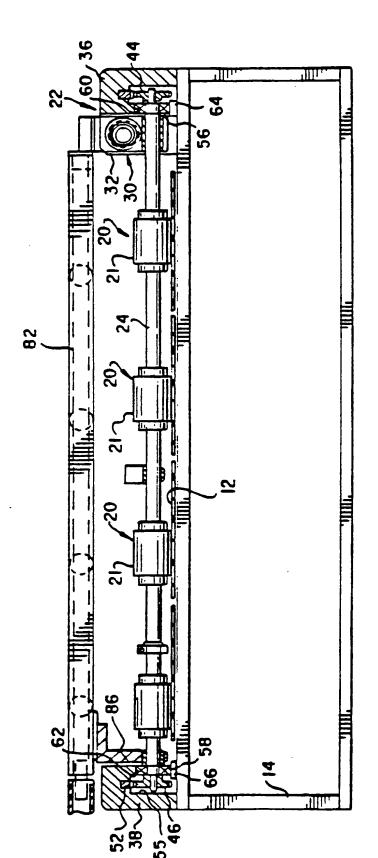
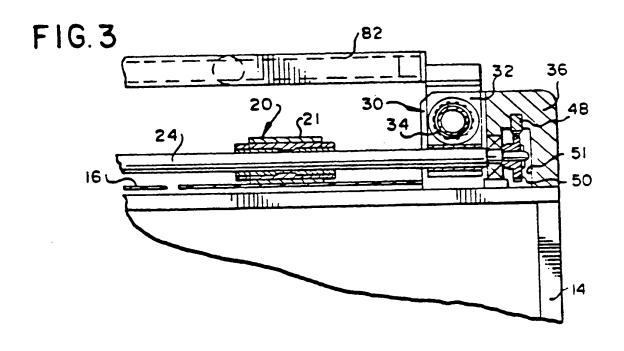
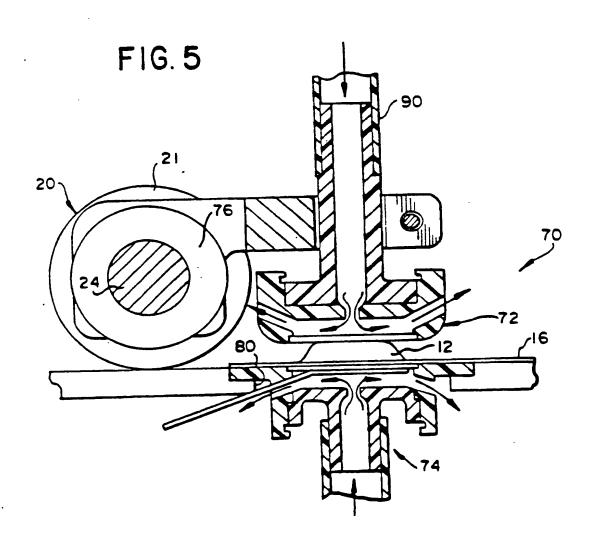
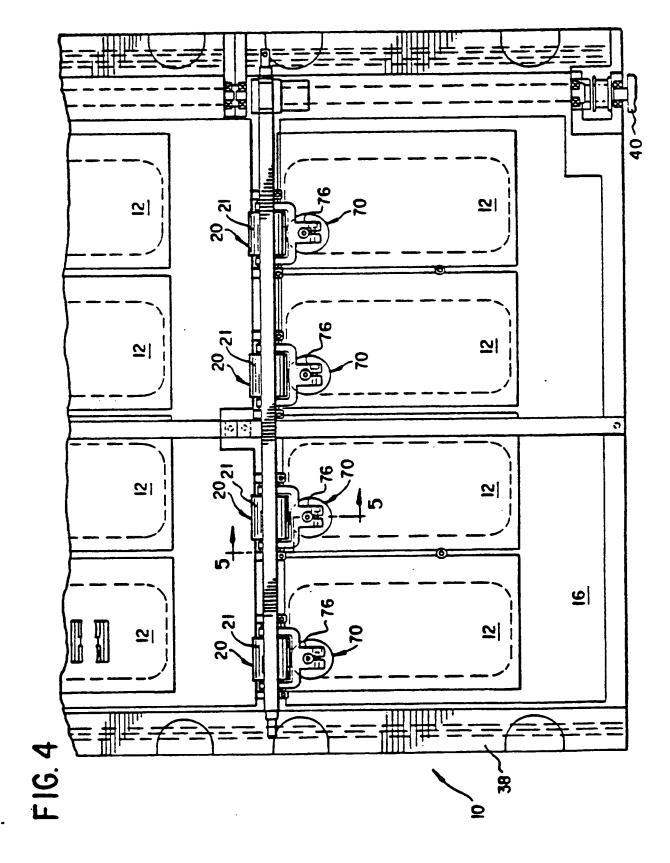


FIG. 2









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apparatus (10) for transferring liquid from one chamber to another in successive chambers of a chemical reaction pack (12). The apparatus (10) comprises a support surface (16) on which the packs (12) are placed, and a plurality of pressure applicators (20) which are driven to apply pressure to the packs (12). Temperature control elements (70) are also provided to heat and cool the liquid contained within each chemical reaction pack (12).

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EUROPEAN SEARCH REPORT

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DOCUMENTS CONSIDERED TO BE RELEVANT				·
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Υ	FR-A-2 612 295 (G. KARC * Page 2, lines 3-26; page 3	HER et al.) , lines 19-34; figures 1,2 *	1,3-6,9	
Y	US-A-2 455 125 (E.H. LAN Figures 1,2; column 1, line column 4, line 8; column 4, 29-37; column 9, lines 9-18	s 12-32; column 3, line 11 lines 54-64; column 8, line		
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				TECHNICAL FIELDS SEARCHED (Int. CI.5)
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